Co-operativity in neurons and the role of noise in brain

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Abstract

In view of some recent results in case of the dopaminergic neurons exhibiting long range correlations in VTA of the limbic brain we are interested to find out whether any stochastic nonlinear response may be reproducible in the nano scales usimg the results of quantum mechanics. We have developed a scheme to investigate this situation in this paper by taking into consideration the Schrodinger equation (SE) in an arbitrary manifold with a metric, which is in some sense a special case of the heat kernel equation. The special case of this heat kernel equation is the diffusion equation, which may reproduce some key phenomena of the neural activities. We make a dual equivalent circuit model of SE and incorporate non commutativity and noise inside the circuit scheme. The behaviour of the circuit elements with interesting limits are investigated. The most bizarre part is the long range response of the model by dint of the Central Limit Theorem, which is responsible for coherent behaviour of a large assembly of neurons.

1 Introduction

Nervous systems use electrical signals which propagate through ion channels which are specialized proteins and provide a selective conduction pathway, through which appropriate ions are escorted to the cell's outer membrane. Also, the ion channels undergo fast conformational changes in response [1] to metabolic activities which opens or closes the channels as gates. The gating essentially involves changes in voltages across the membrane and ligands. The voltage dependent ion channels have an ability to alter ion permeability of membranes in response to changes in transmembrane potentials. The channels which are Na, K and Ca voltage gated or synaptic channels gated by acetylcholine, glycine or γ aminobutyric acid seemed similar. The magnitude of current across membrane depends on the density of channels, conductance of the open channel and how often the channel spends in the open position or the probability. Hodgkin and Huxley [2, 3] accounted for the voltage sensitivity of Na$^+$ and K$^+$conductance of the squid giant axon by postulating charge movement between kinetically distinct states of hypothetical activating particles. In spite of the detail electrophysiological studies, the atomic structure of voltage gated ion channels still remained in the dark till the discovery of Mckinnon and his collaborators [4, 5, 6] which obtained a crystal structure of a Ca^{2+} gated K^+ ion channel provides a mechanism for gating [7, 8].A functional study of $KvAP$ in this context led to a proposal known as the voltage sensor paddle model. Ion channels are membrane-spanning proteins with central pores through which ions cross neuronal membranes. The pores through each ion channel flicker between open and closed states, starting and stopping the flow of ions and the electrical current they carry.

Considering the voltage sensor capabilities of the ion channels and generation of currents and potentials, we in this paper deal mainly with the electrical properties of the ion channels. It is already known that the neuron acts as an electrical device, [9] where a potential difference develops across the membrane due to differences in ion concentrations between inside and outside the cell. The participating ions are Sodium(Na^+), Potassium (K^+), Calcium (Ca^+) and Chlorine(Cl^+). Nernst equation describes equilibrium potential for a single ionic species as $E = \frac{RT}{zF} ln \frac{[X^+]_o}{[X^+]_i}$. Total membrane current is given by the sum of individual channel currents

$$I_m = I_{Na} + I_K + I_{Cl}$$

In this way, a membrane patch can be described by an equivalent electrical circuit component. As we have discussed earlier, electrical signals are changed in the membrane potential at specific sites of the neuronal network, which are obtained by changes due the closing and opening of ion channels. Given these things to be known, the main objective of this paper is different. First of all in a recent article [10] it has been hypothesized from dimensional arguments that quantum mechanics may be operative at some scale in the ion channels. If this is the case then the whole story of voltage sensing in ion channel gets a new paradigm shift. If we assume that membrane voltage and currents are generated through equivalent circuits but at length scales where quantum mechanics is assumed to hold, then due to noncommutative effects the whole concept of devising electrical circuits is different, but also at the same time it should be mentioned here that at large length scales corresponding to a large collection of ion channels in comparison to a single or few ion channels in the previous case, we expect the quantum effects to average out and the conventional circuit elements for describing the mechanisms of voltage [11, 12] and current generation through the gates is valid.

In this paper, we implement a quantum circuit for the ion channels following the lines of [13]. The fundamental assumption has been that, Hodgkin and Huxley's empirical, deterministic model may be reformulated where the relevant behaviour arises from the combined contributions of a large number of small stochastic components. Our model averages away the random behaviour at the smallest scale.Our intention in this paper is to set up rigorously the underlying stochastic process of one such model and then to prove that its behaviour converges to that predicted by the earlier deterministic model as the limit is taken in a suitable regime, in that the sample paths of the stochastic process converge in probability to the trajectory predicted by the deterministic model. Stochastic Hodgkin-Huxley model relates behaviour on three distinct scales, the flow of charge at the scale of individual ions, the opening and shutting of ion channels at the scale of large protein molecules and the working of the whole axon. The

basic task in hand is as follows, we have developed a Schrodinger equation and a implementation of the equivalent circuit. Now following the work [14] on neuromanifolds we assume that the underlying geometry of the ion channels is not known a priori. Thereby we assume a curved manifold and write down the nonlinear Schrödinger equation (NLSE), essentially a heat kernel equation in a curved manifold [15]. The next task in hand is to find out an equivalent circuit model for that. In the last section we find out a connection with the HH model and determine how the quantum effects may get lost at large length scales in the mesoscopic case when we take the limiting case of large number of ion channels. Thus we can think of the difference between the stochastic and deterministic models as one of resolution: although neither model can 'see' the individual ions, the stochastic model can see single channels, whereas even these are beyond the deterministic model. In this sense the main result of this paper is a check that if we average out over the smallest scale to obtain the stochastic model, and then consider a suitable limit of this to represent the vanishing size of the intermediate scale, we recover the model obtained by averaging over both smallest and intermediate scales from the start.So essentially in this paper we are confronted in understanding the dependence of noise and co-operative effect of the neuronal architecture on the spatial and temporal scales in the brain.

2 Role of Noise & Cooperativity in Hodgekin-Huxley(HH) Formalism

Following the study of Hodgkin and Huxley, most of the models of axons have treated the generation and propagation of action potentials using deterministic differential equations. Since [16] it has become increasingly evident, however, that not only the synaptic noise but also the randomness of the ion channel gating itself may cause threshold fluctuations in neurons [17, 18]. Therefore, channel noise which originates in the stochastic nature of the ion channel dynamics should be taken into account [19]. For example, in mammalian ganglion cells both the synaptic noise and the channel noise might equally contribute to the neuronal spikes variability [20]. Due to a finite size, the origin of the channel noise is basically due to fluctuations of the mean number of open ion channels around the corresponding mean values. Therefore, the strength of the channel noise is mainly determined by the number of ion channels participating in the generation of action potentials. Channel noise impacts, for example, such features as the threshold to spiking and the spiking rate itself the anomalous noise-assisted enhancement of transduction of external signals, i.e. the phenomenon of stochastic resonance [21, 22, 23], and the efficiency for synchronization.

When an ion channel opens or closes, an effective gating charge is moved across the membrane. This motion creates the so-called gating current which is experimentally measurable [24]. The influence of gating currents was not explicitly considered in the original Hodgkin-Huxley (HH) model. The model we would like to describe is a neuronal model at length scales of ion channels where we believe that quantum mechanics may be operative. But we believe that the model may also include the HH model as a special case where coarse graining can be done, or for example, if we include large number of channels, the collective behaviour should be described by the HH model. For the sake of completeness, we would like to describe the HH model in brief [25].

In the HH case, the basic membrane circuit suitable for, say, a squid giant axon with two voltage dependent channels is given by the following construction: The circuit is described by a capacitor C, sodium, potassium, leakage conductance G_{Na}, G_K and G_L respectively. The membrane potential is the voltage difference between the outside and inside of the cell membrane and there can be a current injected into the cell from an electrode or other parts of the cell.

The equations describing the phenomena is given by

$$C\frac{dV}{dt} = I_{ext} - G_{Na}(V - E_{Na}) - G_K(V - E_K) - G_L(V - E_L) \tag{1}$$

G_{Na} and G_K are the functions of membrane potentials and time and are given by the

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following equations,

$$G_{Na} = \overline{G_{Na}}m^3h \quad \frac{dm}{dt} = \frac{m_\infty(V) - m}{\tau_m(V)} \quad \frac{dh}{dt} = \frac{h_\infty(V) - h}{\tau_h(V)} \tag{2}$$

$$G_K = \overline{G_K}n^4 \quad \frac{dn}{dt} = \frac{n_\infty(V) - n}{\tau_n(V)}$$

$$\tag{3}$$

Here m^3h, n^4 can be interpreted as the opening probability of a channel. The Na channel has two set of gates i.e., activation gates represented by m and inactivation gates represented by h. The activation gates open and the inactivation gates close when the membrane depolarizes. The K channel has only single activation variable which is a 4 parameter system.

So we see that the state vector variables of the HH model are V, m, h, n. The equations [1,2,3] can be written in a compact matrix notation as

$$\dot{\overrightarrow{X}} = \overrightarrow{F}(\overrightarrow{X}) \tag{4}$$

where $\overrightarrow{X} = [V, m, h, n]^T$. Equation [4] is a nonlinear equation and mainly numerical methods are employed in solving such equations. We will not go into details of those analysis as here we are interested to carry out the analysis in terms of the relevance of quantum mechanics in ion channels [26, 27] and develop a framework for that and then to see if there exist any limit for which it will reduce to the HH model. In understanding the noise in ion channels apart from the thermal background noise we can look into the phenomena through the stochastic nature of closed(C) and open(O) states with a distribution functions[28],

$$\frac{O}{O + C} = \frac{1}{1 + exp[w_0 - zeE]} \tag{5}$$

where w_0 is the conformational energy in absence membrane potential, z is the gating charge and E the membrane potential. We speculate the possibility of stochasticity arising out of closed and open channels. There has been an interesting result related to the Runge Kutta numerical implementation of noise terms [29, 30] which are stochastic in nature associated with some random numbers given by

$$\Delta\eta = \sqrt{4\Delta t log(r_1)}cos(2\pi r_2)$$

More interestingly, the observation that understanding ion channel dynamics is stochastic in nature has prompted us to look at the relevance or analog of stochasticity in the quantum case. A similarity of the HH model with the cellular automation has been observed, [29, 31, 32] which in the limit of large ion channel density gives rise to a Langevin description. Using the Stratonovich description, the HH model is rewritten in the Langevin form as

$$\frac{d}{dt}x_i = A_i(x) + B_{ij}\eta_j(t) \tag{6}$$

where $i, j = 1 \cdots n$ for the n channels and A_i, B_{ij} are related with the moments of the underlying transition probability.

It is striking that HH formulation yields into a noisy model in the large ion channel number limit. This observation has become very crucial in our proposal of the general formulation of the HH formalism in the quantum case. The most important theoretical result we are hinting is the role of noise which is manifest in the brain due to some functional geometry which is the underlying structure assumed in the brain structure. The justification at this stage will demand serious experimental investigations which will explore the dependence of phenomena at various length scales.

We do also propose a new model based on the cooperative activation of sodium channels that reproduces the observed dynamics of action potential initiation. In vitro experiments confirm this prediction, [33] supporting the hypothesis that cooperative sodium channel activation underlies the dynamics of action potential initiation in cortical neurons. The rapid onset of action potentials is independent of the temporal structure of synaptic inputs and of

the electrophysiological cell class. It seems that rapid action potential onset and large variability in onset potentials are strongly antagonistic in HodgkinHuxley-type models. In such models, the initial phase of an action potential is determined by the activation of voltage-dependent sodium channels. Their dynamics is described by the activation curve and kinetics of an associated gating variable. In the HodgkinHuxley formulation it can be shown that the rate of membrane depolarization is limited by $g_{Na}hm^3(V)(V_{Na} - V)/C + I_o/C$, where g_{Na} denotes peak sodium conductance, h is the fraction of sodium channels available for activation, $m^3(V)$ is their activation curve, V_{Na} is the sodium reversal potential, C the membrane capacitance, and I_o is the current carried by other channels. It is plausible that there is a one-to-one relationship between the single-channel activation curve and the action potential onset dynamics, owing to the assumption that the opening of individual sodium channels is statistically independent. This assumption, however, might be violated in the highly organized molecular machinery of a living cell [34]. Indeed, the rapid onset of action potentials suggests that many sodium channels open virtually simultaneously, that is, in a potentially cooperative fashion.

To assess whether cooperative activation of voltage-gated sodium channels can account for the two characteristic features of cortical action potential initiation, a model of a population of coupled sodium channels was constructed. Assuming that channel interactions are distance-dependent in neuronal membranes, the model predicts gradual recovery of the number of available sodium channels during washout of TTX led to a gradual increase in action potential onset rapidness. These results cannot be explained by HodgkinHuxley-type models, in which reduction in the sodium channel density modifies only the amplitude of action potentials and their onset potential, but not their onset rapidness.

3 Nature of Brain Processes

It is really debatable at this stage to pin the nature of brain processes. Inspite of the minuteness of the ion channels or the neurons, it really seems that decoherence effects will nullify the quantum effects of the neurons as a whole. But in the light of recent discoveries on , cooperative phenomena and some stochastic dynamics in ion channels, it is really true that even quantum effects in single ion channels, will cumulatively give rise to some hitherto unknown classical states. As an example we have summarized decoherence processes in ion channels due to some fundamental processes.

	Object	Environment	t_{dec}
Decoherence timescales.	Neuron	Colliding ion	10^{-20}s
	Neuron	Colliding *water*	10^{-20}s
	Neuron	Nearby ion	10^{-19}s
	Microtubule	Distant ion	10^{-13}s

The results may enable us to address the question of whether cognitive processes in the brain constitute a classical or quantum system. Neuron firing itself is also highly classical, since it occurs on a timescale $t_{dyn} \sim 10^{-3} - 10^{-4}$ *seconds* [35].But the problem with such approach is closely related to assuming that there is a unique timescale associated. For example if we admit a quantum description inside the ion channels then, because of the uncertainities introduced at the ionic level, the brain state will develop into a continuos distribution of virtual macroscopic states.

4 Stochastic geometry in Neuronal Modeling

Very Recently the (Nonlinear Schrodinger Equation) NLSE has been solved with an artificial neural network scheme. This analysis gives us an insight and assurance that maybe the NLSE will play an important role in analyzing realistic neuronal modeling. Here we discuss in brief about the solution of NLSE on a network.

The time dependent propagation of light pulse inside a single mode nonlinear optical fiber

is given by the solution of

$$i(\frac{\partial \Psi}{\partial z}) - \alpha(\frac{\partial^2 \Psi}{\partial z^2}) - \beta\|\Psi\|^2\Psi = 0 \tag{7}$$

where Ψ is the field amplitude, z and t are the optical and time axis respectively, α, β are the dispersive and waveguide coefficients respectively. The competition between pulse dispersion and focussing gives rise to the formation of solitons for a particular input. With suitable boundary conditions a stable soliton is obtained. It has been observed that the solution consists of a 3 layer architecture with 42 hidden nodes [36]. Now to speak of the implications of this result it has been also observed that the knowledge of the upper bound on the field amplitude provides a stopping criterion on the training of the neural network (NN).

We present a model where the propagation of activity is stochastic and the connections are random. Each excitable element $i = 1, \ldots, N$ has n states: $s_i = 0$ is the resting state, $s_i = 1$ corresponds to excitation and the remaining $s_i = 2, \ldots, n-1$ are refractory states. There are two ways for the i-th element to go from state $s_i = 0$ to $s_i = 1$: a) due to an external signal, modelled here by a Poisson process with rate r (which implies a transition with probability $\lambda = 1 - \exp(-r\Delta t)$ per time step); b) with probability p_{ij}, due to a neighbour j being in the excited state in the previous time step. Time is discrete (we assume $\Delta t = 1$ ms) and the dynamics, after excitation, is deterministic: if $s_i = 1$, then in the next time step its state changes to $s_i = 2$ and so on until the state $s_i = n-1$ leads to the $s_i = 0$ resting state, so the element is a cyclic cellular automaton, [37, 38, 39]. The Poisson rate r will be assumed to be proportional to the stimulus level S .

Two kinds of oscillations are observed in the system. Under sufficiently strong stimulation, *all* networks present transient collective oscillations, with frequencies of the order of the inverse refractory period. They are a simple consequence of the excitable dynamics and the sudden synchronous activation by stimulus initiation. The transient behaviour is reminiscent of oscillations widely observed in experiments[40], but its trivial origin suggests that they are epiphenomenal and without computational relevance. Networks with $\sigma > \sigma_{osc} > \sigma_c$ also present self-sustained oscillations in the absence of stimulus where σ_{osc} is a bifurcation threshold. The frequency depends on the network parameters, but remain in the gamma range. The oscillations are similar to reentrant activity found in other models of electrically coupled networks[41].

It may be pertinent to ask at this stage that what use is of the above scheme to our proposed model. What we believe is that applicability of NLSE on NN gives us a clue that may be the Schrödinger equation is applicable at diverse length & temporal scales in neuronal architecture with an unknown, a priori geometry and the basic objective is to find out the appropriate dynamics for that.

We have already emphasized that the neuronal architecture has a form of geometry with some probabilistic structure on it giving rise to a probabilistic manifold [42]. So the main point of the analysis depends on the identification of a stochastic interpretation to quantum mechanics. The essential ingredient is following. We claim that the operator $A = b_\nu(x)\partial_\nu + (\frac{\hbar}{2\pi i})\nabla$ is the infinitesimal generator of the stochastic process defined by the Langevin equation

$$dx_\mu(t) = b_\mu(x,t)dt + dW_\mu(t) \tag{8}$$

The importance of this identification is that classical probability theory gets related with quantum mechanics. Now, the next question what we can ask is that we are trying to define the SE in a curved probabilistic manifold. So, apart from a stochastic approach to quantum mechanics ,we need something more, i.e., to randomize the metric. Let us assume a Lagrangian, given by

$$L = \frac{m}{2}g_{\mu\nu}(x)\dot{x}_\mu\dot{x}_\nu - V(x) \tag{9}$$

Variation of this Lagrangian gives us the equation of motion in the form of geodesics. If we vary the trajectories and define a stochastic process in terms of the variations with gaussian spread and compare this distribution with the Feynman path integral, we end up with the Riccati equation which is the stochastic analogue of the Schrödinger equation on a curved

manifold.

$$\frac{\hbar}{2}\nabla_\mu x^\mu + \frac{m}{2}x^\mu x_\mu = V + \frac{\hbar^2 R}{6m} \tag{10}$$

So we see that stochasticity [43] involves a generation of an effective potential of motion. We will see now that how this may be handled in analyzing the quantum circuits.

5 Rules of Design through Cooperativity & Quantum Mechanics

It is indeed true that in understanding neural mechanisms, we need nonlinear and dissipative analysis. Now as has been argued in [44] over the years and until recently, if we think of the relevance of quantum mechanics and the role of Cooperative phenomena for neuronal dynamics at suitable length scale. For an atom in a cavity, a process such as spontaneous emission is sometimes viewed as dissipative but if some number of modes are chopped of, the process becomes reversible. In comparison, the resistance to electric current flow is reversible, which is typical of closed system. But if we think of quantum circuits the situation is drastically different.

In this context, we cite an particular example: A current driven RC circuit which is identical to a free particle driven by an external force. In absence of the resistor, the system is well described by the charge operator Q and operator ϕ which satisfy $[\phi, Q] = i\hbar$. We would like to mention here that a circuit theory [45, 46] that can describe quantum transport, is particularly important and has potential applications in nanotechnology, molecular devices and beam epitaxy etc [47].

As we have already seen that the electric charges of ions are in fact responsible for the membrane potential and action potential. Generation of the potential therefore gives rise to the possibility of modeling the ion channels through electric circuits, which generate the required potentials. The scheme is devised through a quantum analogue of the corresponding electrical circuit. So our objective is pretty clear. Some very recent results at ionic scales regarding the relevance of Quantum Mechanics (QM) [48], we try to build some viable neuronal models and corresponding electric circuits [49]. But as QM governs the dominant dynamics we have to develop quantum circuits.

In this context, we would like to mention very important work [13] which we earlier mentioned, related to the circuit equivalent of Schrodinger's equation. The circuits were originally designed for completely different purposes and had no connection with brain activity. It is a way to measure the eigenvalues, eigenvectors and statistical means of various operators, belonging to the system which are being modeled by electrical means. We briefly discus below the scheme for handling those things.

Let the wave equation be divided by $i\omega_c$ where $\omega_c = \sqrt{\omega} = (E/\hbar)^{\frac{1}{2}}$ and multiplied by $\triangle x$ we get

$$-\frac{1}{\omega_c}\frac{\hbar^2}{2m}\frac{1}{\triangle x}\frac{\partial^2 \psi}{\partial x^2}\triangle x^2 + \left(\frac{V\triangle x}{i\omega_c} + \hbar i\omega_c\right)\psi = 0 \tag{11}$$

We should like to note some salient points here.

- The Kinetic energy operator T is represented by a set of inductors in series whose inductance is given by $L_1 = \frac{2m}{\hbar^2}\triangle x$.

- The potential energy operator V is represented by a set of unequal coils in parallel whose inductance is $L_2 = 1/V\triangle x$.

- The total energy operator $-E$ is represented by a set of equal capacitors whose capacitance is $\hbar\triangle x$.

- The operand ψ is represented by voltages and the result of the operation $\alpha\psi$ where α is any operator, is represented by currents.

This model can also be extended to nonorthogonal coordinates and in general on arbitrary manifolds. Utilizing the circuits, tests were carried out on an ac network analyzer. The results are worth mentioning. The tests were done in 1-dimensional circuits. or example

measurements were made for a particular case of the rectangular potential well and analyzed which had good agreement with the experimental results [50].

For the sake of completeness, we should like to mention here that from the preceding model, we can develop a prescription for developing a electric circuit equivalent for the Schrödinger equation (SE). The SE has some analogies with the heat conduction equation

$$\frac{d\psi}{dt} = \frac{1}{\hbar}\Big(\frac{\hbar^2}{2m}\nabla^2 + V\Big)\psi \tag{12}$$

Now we make a prescription for the electric circuit as equivalent to the Schrödinger equation as

$$V \Leftrightarrow \psi \quad \frac{1}{r} \Leftrightarrow V\triangle Vol \quad \frac{1}{Rx} \Leftrightarrow \frac{\hbar^2}{2m}\triangle Vol/(\triangle x^2) \quad C \Leftrightarrow i\hbar\triangle Vol \tag{13}$$

The construction relies here on having N imaginary capacitance and one of the consequence is we will get solutions of the form

$$\psi \sim \exp(ikx)\exp(i\omega t)$$

. Physically this means that we don't have exponential decay with time into thermal equilibrium but we get everlasting solutions which conserve $|\psi|^2$. So we see that if we impose ccoperativity into the picture using theory of resonances, and by dint of central limit theorem, it is plausible to get the required behaviour of non solitonic behaviour corresponding to the fields.

6   Quantum Circuits at Nano Length Scales

Motivated by the quantum mechanical considerations and the circuit equivalence of Schrödinger equation we will now try to formulate an equivalent circuit for the membrane potential in the ionic channels. We will consider a single ion channel and consider the circuit implementation for it. But there are some subtleties regarding this. Tensor network theory [51] may be realized in the brain and there is possibility of a non trivial geometrical structure inside brain as mentioned in [52, 53, 54], work also points towards this direction. This implies that there is an underlying geometrical structure inside brain and it may be important at the ionic scales. So we try to develop a formalism for describing that. We start with some simplifying propositions:

- There is an underlying geometry inside brain which is responsible for neuronal activities and the geometry can be described by a metric.

- Quantum mechanics is applicable at the length scales of ionic channels and the phenomena can be described by Schrödinger equation

- The phenomena at those length scales is stochastic.

With these propositions we can now think of a formalism for various set of events inside the brain. It should be mentioned here that ultimately we would like to connect our formalism to the HH formalism, which has been successful in describing the membrane gating and dynamical phenomena involving channels [55].

So we start by writing a SE equation on a curved manifold. The equation can be identified with a Heat Kernel equation.

$$i\hbar\frac{\partial\psi}{\partial t} = \frac{1}{\sqrt{g}}\partial_\mu(\sqrt{g}\partial_\mu\psi) + V\psi \tag{14}$$

The equation above, for arbitrary metric, is in general, nonlinear and in accordance with our third proposition we claim that the processes are stochastic in nature and the analysis of section 4 tells us that the dynamics will be governed by Riccati like equation [10] with a correction in the potential term as

$$i\hbar\frac{\partial\psi}{\partial t} = \frac{\hbar^2}{2m}\nabla^2\psi + (V + \frac{\chi(q)\hbar^2\sqrt{N}\vartheta}{6})\psi \tag{15}$$

ϑ is the curvature scalar, associated with the metric, which gets incorporated into the potential term. It is important to note that the correction term differs from that of equation [10] in a coordinate dependent factor. We will show that this factor is crucial in developing a quantum equivalent of a circuit. The mass is absorbed in the coordinate dependent term. The χ in some sense acts as a space modulation factor which governs both the noncommutative aspects and the fluctuations from the metric.It should be mentioned here that this equation describes the dynamics for N channels and we have made a conjecture by including the number of channels, with a hope to get the classical picture of the HH equation in global limit.

The Schrödinger equation along with the correction of the quantum term is a good starting point in our case to develop a circuit equivalent. Actually the problem in this case to extend the previous construction for the equivalence of SE to electrical circuit is dictated by the presence of the metric. First of all, the metric is a dynamical variable which governs the behavior of space time. So, we cannot just implement it as some electrical component, since such a component should have the ability to shape the global structure of the full circuit. At the moment, we do not know of any such component. We have seen that in periodically driven circuits, we can scale the capacitance or say the inductance as $L \sim \gamma g(t)$ which may capture, in some sense, the global dynamics, but it will not catch the full glimpse of the dynamical behavior. The curvature gets into the potential term and thereby fluctuations in the metric will induce different potentials and hence only periodic variations may not do [56, 57]. It is a widely held that fundamental processes of nature may be explained by probabilistic metric and the probabilistic features can be modeled into uncertainties or fluctuations from a physical point of view. If we introduce the fluctuations in the metric as

$$g_{ij}(x,h) = g_{ij}(x) + \alpha_{ij}(h)$$

the fluctuation of the metric generates a random potential V, a random coefficient S which depends on the fluctuations. In the quantum case we will do indeed get dissipation which depends on the fluctuation. The Schrödinger equation turns to be

$$\frac{\hbar^2}{2}\frac{\partial^2\phi}{\partial r^2} + V\phi = S\frac{\partial\phi}{\partial t} \tag{16}$$

To make connections with brain activities and neuronal circuits we try to develop circuits corresponding to quantum mechanics, the circuit will do contain some flavor of the noncommutative aspects.

We know that brain phenomena is considered as dissipative. In such kind of theories, one considers such one partcle dissipation in quantum theory. So, we try to extend that formalism in our case with the corrected potential along with a source term. Then we consider the following Hamiltonian as:

$$H = -e^{-Rt/L}\frac{\hbar^2}{2e^2L}p^2 + e^{Rt/L}(\frac{1}{2C}q^2 + \varepsilon q + \frac{\chi(q)\vartheta\hbar^2\sqrt{N}}{6}) \tag{17}$$

Here q is state variable, p the conjugate which goes uplifted to the charge operator when we deal with quantum mechanics (QM). Using the Heisenberg equation of motion, the equation for the state variable is given by

$$L\frac{d^2q}{dt^2} = \frac{1}{2e^2}(\{\frac{1}{2C}q^2 + \varepsilon q + \frac{\chi(q)\vartheta\hbar^2\sqrt{N}}{6}\}, [p^2, q]) - R\dot{q} \tag{18}$$

So, evaluation of the simple commutator gives us the equation for the corresponding quantum circuit as

$$L\ddot{q} + R\dot{q} + \frac{q}{C} = \varepsilon + \frac{\alpha\hbar^2\sqrt{N}}{6}\vartheta\dot{q}\int dt\chi'(q) \tag{19}$$

The last term in the above equation is most striking. It shows that that the above equation clearly shows that the inductance gets corrected, by a quantum term. In this way, ultimately, at the level of circuit equivalence, we will be getting a renormalized inductance. It gives

the equation a status of an integral equation and would be interesting to find out the conditions under which it will reduce to a differential equation. In that case, the capacitance gets renormalized.

It is very important so as to make some measurements to find out these extra factors. There is an extra parameter in the theory which needs to be fine tuned to get the desired effects. The above equation can also be transformed into a Langevin like form and get a measure for the Probability functional, which is very non trivial due to the presence of the curvature term and may hint at some statistical manifold like character. This is not quite surprising as we mentioned at the beginning of the section that it may arise due to the intrinsic stochasticity of the neuronal activities. The above observations have some interesting consequences with respect to Nonlinear Schrodinger Equation. Some of the results is worth mentioning . If we had included in the Schrödinger equation a damping factor in the form of a bounded negative operator and a quasi periodic force, the solutions turn out to be even and periodic. The analysis in such case, give rise to the existence of invariant manifolds in the phase space of the equation. The infinitely many eigenvalues in the integrable limit turn into complex eigenvalues with negative real parts. The manifolds exhibit a dynamical behavior and the geometry resembles those of certain homolinic orbits in finite dimensional Ordinary Differential Equation [58].

7   Determinism as a limit of Underlying Stochastic Processes

It is now pertinent to understand how the stochastic quantum phenomena at ionic scales by decohorence effects give rise to determinism of the HH models. The instantaneous electrical state of the axon depends on the locations and internal states of any molecular mechanisms at work in the axon and in particular ion channels.As we have mentioned before the stochastic model describes the working of individual ion channels, whereas the deterministic model 'averages out' their behaviour, involving instead functions that describe the proportion of those channels in a small neighbourhood of a point that are in each possible state.

The state of our system is partly described by a function $v : I \to \mathbf{R}$ giving the value of the membrane potential at each point along the axon. Since ions can diffuse along the axon, the variation of this function with time will also exhibit diffusive behaviour, allowing us to impose certain regularity conditions on it. Our model involves a renormalization of ionic conductivities corresponging to each ion channel pore. Assuming all channels as identical, as described above, in our model the driving potentials will actually correspond to the different possible channel states $\xi \in E$, the space of states. The stochastic model implies that a channel at position x will jump between states ξ, ζ at random at specific rates $\chi_{\xi,\zeta}(V)$, where V is the value of the potential difference at the relevant point x. So there will be one such model for each $N \in \mathbf{N}$. The deterministic model arises heuristically as the limit of the stochastic model with very many very small ion channels; that is, for large N. In the deterministic model a new family of functions $p_\xi \in \mathrm{Lip}(\mathrm{I}, [0,1])$ for $\xi \in E$, may be introduced that replicates the role of the individual-channel configurations. The value $p_\xi(x)$ is to be interpreted as the proportion of those channels in a small neighbourhood of the point x that are in state ξ.

8   Conclusion

The primary observable of an ion channel is its conductance. Because the channel current depends on both applied voltage (V) and bath concentrations (C) and the conductance data is typically plotted in the form I-V & I-C Curves. We need to estimate in our case the conductivities for the ion channels from the curves, which follows non-linearity, upto an appreciable range. Simulation model studies have indicated that the non-linearities arise as a result of residual energy barrier in the channel. A Quantum Jump approach analogy for understanding how the dynamics of Stochastic Schrödinger Differential Equation induces cooperative mechanism using the damping of one field mode in a cavity at temperature T can also be given.

The striking aspect of our result is that in the most general case, for scales in which QM is applicable, we have found out a generalized HH equation with the conductances G_A being corrected with the renormalized value in equation [1] by

$$G_A + (\frac{\alpha\hbar^2\sqrt{N}}{6}\vartheta\dot{q}\int dt\chi'(q))^{-1}$$

It is necessary to study following two issues. Firstly, to see under what limit does this modified equation i.e., generalized HH equation turns to ordinary equation with no renormalization. Then, one needs to do the experiments to see whether the conductances indeed do get corrected. If it is so then we could measure such term for single ion channels. We also believe that one of the mechanisms by which we may get ordinary HH theory with no renormalization (i.e quantum mechanics is unimportant) is when there are many channels and quantum mechanics is getting subdued in the large N limit. Anyway, there is a subtle point here. In confirmation of the relevant observation for the stochasticity of HH equation in the Langevin description, we see that in the classical limit, we may get stochasticity for a critical large value of the number of channels. It is really important to design experiments to measure critical parameters as appeared in the above equation. Such experiments will be very conclusive for the correctness of the model and also give a direct evidence for the applicability of QM in ion channels. It is also crucial to measure the effective conductance. At this stage, we still do not know how we can model such mechanisms, but experimental results on single ion channel may surely shed some light in understanding these aspects [59, 60, 61, 62].

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